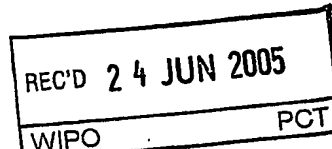


PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY



To:

see form PCT/ISA/220

28/7

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2005/000168

International filing date (day/month/year)
10.01.2005

Priority date (day/month/year)
08.01.2004

International Patent Classification (IPC) or both national classification and IPC
C07F19/00, C07D487/22, A61K49/00

Applicant
UNIVERSITÄT ZÜRICH

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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Authorized Officer

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/000168

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☐ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:
see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/000168

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 13

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 13
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☒ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/000168

Box No. V Reasoned statement under Rule 43*bis*.1(a)(I) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-12,15,16
	No: Claims	14
Inventive step (IS)	Yes: Claims	3-10, 16
	No: Claims	1,2, 11-13, 14,15
Industrial applicability (IA)	Yes: Claims	1-16
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

and /or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

see form 210

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item II

Priority

Only claims 3-10 enjoy the priority right of 12/01/04 in full scope. All other claims have the filing date as the priority date.

D1 published on 27/09/04 is, therefore pertinent prior art (at least partly) in respect of claims 1,2,11-16.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

No search has been carried out for claim 13 because it lacks clarity and its scope in particular with respect to the definitions of L and L' is virtually unlimited.

The only exact definitions are M and n which are common definitions in coordination chemistry.

Functional definitions are sometimes allowable in the claims. However, according to Guidelines C-III, 4.7, a functional definition can only be considered clear according to Art. 6, PCT where:

- (1) the invention cannot otherwise be defined without unduly limiting the scope of the claim and
- (2) the functional definition can be reduced to practice by the skilled person without undue burden, if necessary with reasonable experiments.

In the case of the present claim 13, the functional feature for L used to define the solution to the technical problem, is the partly the problem itself. This formulation covers all future solutions to the problem, which means:

- (a) The scope of the claimed invention would **not** be unduly limited by including technical features of the claimed compounds, since it is clearly not an undue limitation of the claim to eliminate what has not yet been invented
- (b) A skilled person **cannot** reduce to practice a definition of the claimed subject matter because the complexes comprised by claim 13 have potentially limitless structural possibilities, and so there is absolutely no limit to the structural variation in the complexes which might be useful as an intermediate.

Consequently the requirements of Guidelines C-III, 4.7 whereby a functional definition might be allowed are clearly not fulfilled and so claim 13 is not clear.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1 : KUNZE, SUSANNE ET AL: "Vitamin B12 as a ligand for technetium and rhenium complexes" ANGEWANDTE CHEMIE, INTERNATIONAL EDITION , 43(38), 5025-5029 CODEN: ACIEF5; ISSN: 1433-7851, 27 September 2004 (2004-09-27), XP002328039

D2 = EP-A-109677

Novelty

With respect to complexes in which M is Rh, Pd, Pt, Re or Tc the document D1 is no prior art.

The document D1 indicated in the search report as a P(X)-document does not show metal complexes having central ions other than Rh, Pt, Pd, Re or Tc. Hence, the part of independent claim 1 and dependent claims 2, 11, 12, 15, 16 which does not enjoy the priority right of 12/01/04 is novel.

Claim 14 lacks novelty over cisplatin disclosed in D2, page 1, line 11.

Inventive step

D1 already discloses Vitamin B12 complexes having the structural element Co-CN-M (M is Re or Tc); preparation processes and intermediates therefor; see D1, page 5026, column 2 - page 5028, column 1. Use for radiodiagnostics is described at page 5028, column 1 paragraph 2. Other biological applications are described at page 5028, column 1 paragraph 1.

The enlargement of this concept to the use of metals other than Rh, Pd, Pt, Re or Tc lies well within the possibilities of the skilled person.

Hence, claims 1, 2, 11-15 lack inventive step over D1

Re Item VII

Certain defects in the international application

The prior art according to D1 is not mentioned in the description.

Re Item VIII

Certain observations on the international application

As to claim 13; see item III

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 24 JUN 2005

WIPO

PCT

PCT

To:

see form PCT/ISA/220

28/7

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
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FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2005/000168

International filing date (day/month/year)
10.01.2005

Priority date (day/month/year)
08.01.2004

International Patent Classification (IPC) or both national classification and IPC
C07F19/00, C07D487/22, A61K49/00

Applicant
UNIVERSITÄT ZÜRICH

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
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- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/000168

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☐ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.
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3. Additional observations, if necessary:
see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/000168

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 13

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 13
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
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- ☒ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/000168

Box No. V Reasoned statement under Rule 43bis.1(a)(I) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-12,15,16
	No: Claims	14
Inventive step (IS)	Yes: Claims	3-10, 16
	No: Claims	1,2, 11-13, 14,15
Industrial applicability (IA)	Yes: Claims	1-16
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)
and /or
2. Non-written disclosures (Rules 43bis.1 and 70.9)
see form 210

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item II

Priority

Only claims 3-10 enjoy the priority right of 12/01/04 in full scope. All other claims have the filing date as the priority date.

D1 published on 27/09/04 is, therefore pertinent prior art (at least partly) in respect of claims 1,2,11-16.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

No search has been carried out for claim 13 because it lacks clarity and its scope in particular with respect to the definitions of L and L' is virtually unlimited.

The only exact definitions are M and n which are common definitions in coordination chemistry.

Functional definitions are sometimes allowable in the claims. However, according to Guidelines C-III, 4.7, a functional definition can only be considered clear according to Art. 6, PCT where:

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- (a) The scope of the claimed invention would **not** be unduly limited by including technical features of the claimed compounds, since it is clearly not an undue limitation of the claim to eliminate what has not yet been invented
- (b) A skilled person **cannot** reduce to practice a definition of the claimed subject matter because the complexes comprised by claim 13 have potentially limitless structural possibilities, and so there is absolutely no limit to the structural variation in the complexes which might be useful as an intermediate.

Consequently the requirements of Guidelines C-III, 4.7 whereby a functional definition might be allowed are clearly not fulfilled and so claim 13 is not clear.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1 : KUNZE, SUSANNE ET AL: "Vitamin B12 as a ligand for technetium and rhenium complexes" ANGEWANDTE CHEMIE, INTERNATIONAL EDITION , 43(38), 5025-5029
CODEN: ACIEF5; ISSN: 1433-7851, 27 September 2004 (2004-09-27), XP002328039

D2 = EP-A-109677

Novelty

With respect to complexes in which M is Rh, Pd, Pt, Re or Tc the document D1 is no prior art.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2005/000168

The document D1 indicated in the search report as a P(X)-document does not show metal complexes having central ions other than Rh, Pt, Pd, Re or Tc. Hence, the part of independent claim 1 and dependent claims 2, 11, 12, 15, 16 which does not enjoy the priority right of 12/01/04 is novel.

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Inventive step

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The enlargement of this concept to the use of metals other than Rh, Pd, Pt, Re or Tc lies well within the possibilities of the skilled person.

Hence, claims 1,2, 11-15 lack inventive step over D1

Re Item VII

Certain defects in the international application

The prior art according to D1 is not mentioned in the description.

Re Item VIII

Certain observations on the international application

As to claim 13; see item III